AD_____

Award Number: W81XWH-10-1-0935

TITLE: Value of MRI and DTI as Biomarkers for Classifying Acute Spinal Cord Injury

PRINCIPAL INVESTIGATOR: Adam E. Flanders, M.D.

CONTRACTING ORGANIZATION: Thomas Jefferson University
Philadelphia, PA 19107-5543

REPORT DATE: October 2011

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
October 2011	Annual	30 September 2010 – 29 September 2011

4. TITLE AND SUBTITLE

Value of MRI and DTI as Biomarkers for Classifying Acute Spinal Cord Injury

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-10-1-0935

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Adam E. Flanders, M.D.

E-Mail: adam.flanders@jefferson.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Thomas Jefferson University
Philadelphia, PA 19107-5543

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The purpose of this study is to determine if diffusion tensor imaging (DTI) in conjunction with conventional magnetic resonance imaging (MRI) can reliably forecast neurologic recovery after spinal cord injury (SCI). As we are only in our second month of patient recruitment, there are no significant findings to report.

15. SUBJECT TERMS
N/A.

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
U	U	U	UU	12	**19b. TELEPHONE NUMBER** *(include area code)*

Table of Contents

Introduction

Use of MRI/DTI may improve accuracy in stratifying SCI patients that are being selected for clinical trials to test novel therapies. Trials which utilize MRI/DTI at the point of entry have the potential to demonstrate therapeutic efficacy with fewer patients. The objective of our proposal is to prove that the MRI features of SCI and DTI when used in conjunction with the initial neurologic assessment will provide a better method to classify patients during their initial hospitalization and will better discriminate patients that have capacity for spontaneous functional recovery from those with no inherent capacity for recovery. The results derived from this project have the capacity to radically alter the methods by which we categorize SCI at the point of entry into the healthcare system by more accurately characterizing the extent of their injuries and providing the opportunity to administer appropriate therapies in the critical few hours after injury. This has direct benefit to the individual patient and their families in gauging expectations for recovery and in selecting patients for novel therapies. The goal of this study is to combine the information obtained from the physical examination of the SCI patient at the time of injury with the anatomic and physiologic information provided through MRI and DTI to better predict which patients might realize the most benefit from a new medication. If the added value of MRI and DTI improves the pre-selection process of patients for a new medication, this could also provide a secondary benefit in helping to expedite the drug approval process by decreasing the number of patients required to prove that the drug actually benefits patients.

Body

Relevant dates:

- 05/18/2010 – Approval letter from DoD.
- 07/22/2010 – Initial request for IRB approved protocol, IRB approval letter and consent form from DoD for second level review.
- 09/30/2010 – Receipt of funds from DoD and official start date.
- 10/07/2010 (month 1) – 2nd request for IRB approved protocol, IRB approval letter and consent form from DoD for second level review.
- 11/16/2010 (month 2) – Receipt of protocol, CRFs, CVs, IRB training, IRB approval, COI form and project assurance form.
- 12/02/2010 (month 3) – Project review transferred to Peter Marshall CIP at DoD.
- 02/04/2011 (month 5) – Teleconference with Peter Marshall CIP at DoD to clarify protocol.
- 02/23/2011 (month 5) – Protocol queries via email from Peter Marshall CIP at DoD.
- 02/25/2011 (month 5) – Email response to queries from 02/23/2011.
- 02/25/2011 (month 5) – Email request/response for clarification.
- 04/06/2011 (month 7) – Request for additional information from Mr. Marshall CIP at DoD.
- 04/13/2011 (month 7) – Written response returned to DoD regarding request from 4/6/2011.
- 05/13/2011 (month 8) - Request for additional information from Mr. Marshall CIP at DoD.
- 05/25/2011 (month 8) – Response prepared and sent to DoD regarding queries from 5/13/2011.
- 06/15/2011 (month 9) – Request for IRB approval of revised documents from Mr. Marshall at DoD.
- 07/13/2011 (month 10) – Requested documents from 06/15/2011 returned to DoD.
- 07/27/2011 (month 10)– Final DoD approval for patient enrollment received from Kimberly Odam MS CIP at DoD.

All Task 1 items referenced in the SOW were finally completed by month 10 (instead of month 4). Preparation of the protocol (1a), the TJU IRB submission (1b) and submission to the DoD (1c) were completed by month 2. DoD queries returned by month 5 and responses delivered to DoD in same week (1d). We were finally given permission to begin open enrollment on 7/27/2011 (month 10).

Regarding the Task 2 items, only two spinal cord injury patients have been successfully enrolled thus far in the 10 weeks of open enrollment (item 2a & 2d). We have successfully identified the twenty trauma patients with no neurologic deficit who have been screened with MRI as per 2b of the SOW.

For the enrolled patients, all of the Task 3 specifications were completed including the conventional anatomic MRI (3a) and the diffusion tensor imaging acquisition (3b).

For the enrolled patients, the initial clinical assessments were performed (specified in 4a and 4c). Recovery calculations (4b, 4d and 4e) are deferred pending subsequent neurologic assessments.

Assessment of the conventional MRI studies (Task 5) were performed on the two enrolled patients by two neuroradiologists. Length, location and morphology of the cord lesion was recorded (5a, 5b, 5c).

For the two enrolled SCI patients and the twenty patients without neurologic injury, the data was transferred to a custom workstation for post-processing (6a). An automated co-registration algorithm was implemented (6b) to preferentially filter for preserved white matter fibers in each axial section. Slice by slice FA, MD, LD and TD were calculated for each contiguous axial slice covering the

entire cervical spinal cord (6c). Comparative and group analysis (6d) is deferred pending more patient accrual.

This report fulfills the requirement of SOW Task 7b.

Key Research Accomplishments

- Developed a validated, reproducible DTI protocol that request less than five minutes of acquisition time.
- Trained an entire pool of MR technologists to perform the protocol autonomously.
- Developed a data management plan to transfer raw data to the analysis platform.
- Developed an automated quality control process to rapidly process the DTI data to assess for flaw/errors which might prohibit patient enrollment.
- Developed an enrollment strategy with the rehabilitation co-investigators to ensure capture of all potential patient candidates that meet inclusion criteria.

Reportable Outcomes

- Two presentations the American Society of Neuroradiology (ASNR) Annual Meeting, Seattle, Washington, June 2011 (attached) using preliminary data obtained during protocol development.
    - Application of Diffusion Tensor Imaging (DTI) as a Surrogate for Neurologic Deficit in Spinal Cord Injury (SCI) (11-O-886-ASNR).
    - Diffusion Tensor Imaging (DTI) of "Normal Appearing" Spinal Cord in Spinal Cord Injury (SCI) (11-O-1534-ASNR).
- Upcoming presentation at the 2011 Radiological Society of North America (RSNA) Annual Meeting in Chicago, Illinois (attached) using preliminary data obtained during protocol development.
    - Can Diffusion Tensor Imaging (DTI) Replace the Neurologic Examination in Spinal Cord Injury (SCI)? (MSVN51-02).

Conclusion

Although the inadvertent delays in obtaining final DoD approval consumed much of year 1, our team took advantage of the time by testing, re-testing and refining our imaging protocol and analytical tools on retrospective clinical data to ensure that our acquisition methodology and analytical tools are sound.

Reference

Not applicable.

Appendices

Not applicable.

Supporting Data

Not applicable